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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/922,067	08/03/2001	Colin Houston MacPhee	P30693C4X1C1	8753
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EXAMINER

RAO, MANJUNATH N

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/922,067

Applicant(s)

MACPHEE ET AL.

Examiner

Manjunath N. Rao, Ph.D.

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-26, 28-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25, 26, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Sequence error report</u> . |

Art Unit: 1652

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-29-04 has been entered.

Claims 25-26, 28-29 are currently pending in this application.

Applicants' amendments and arguments filed on 4-29-04, have been fully entered and considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn both the rejections under 35 U.S.C. 112, 1st paragraph as lacking written description in view of claim amendments. Next, without acquiescing to applicant's arguments Examiner has withdrawn the rejection of claims under 35 U.S.C. 102(b) mainly due to fact that applicants are not limiting the enzyme to human source and also due to occurrence of reports in the non-patent literature that there is more than one type of the phospholipase A2 enzyme in humans. Therefore all arguments against the above two rejections are now moot.

Art Unit: 1652

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35

U.S.C. 119(a)-(d).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because of the following informalities: Examiner notes that applicants have not updated the relationship of the instant application to its parent applications that have matured in to US patents. Examiner urges applicants to amend said information by providing the US patent number in response to this Office action. Appropriate correction is required.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that the Office has found errors in the most recently filed sequence listing. See enclosed sequence error report for further details. Furthermore it is noted that applicants claim a polypeptide comprising the amino acid sequence corresponding to amino acid residues 271-441 of SEQ ID NO:9 in claim 29. However, even though applicant has included the amino acid sequence while depicting the polynucleotide sequence SEQ ID NO:9, for all practical purposes of searching and entering into the PTO sequence database, SEQ ID NO:9 is considered as only a

Art Unit: 1652

polynucleotide sequence (see line <212> of sequence listing for SEQ ID NO:9 where it is identified as DNA). If applicant intends to claim the polypeptide sequence depicted as part of SEQ ID NO:9, it is suggested that they file the amino acid sequence only as a separate sequence with a new SEQ ID NO. Without such separation, the sequence claimed in claim 29 cannot be searched. Applicants attention is also drawn to the Sequence Error report enclosed herewith. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 recites the phrase “amino acid sequence corresponding to amino acid residues 271 to 441 of SEQ ID NO:9”. The metes and bounds of the above phrase specifically in the context of the above claim and more specifically with respect to the sub-phrase “corresponding to” is not clear to the Examiner. It is not clear whether applicants are claiming an enzyme comprising said amino acid residues or a variant sequence of the same rendering the claim indefinite. Furthermore, applicants provide a single SEQ ID NO: for both the amino acid sequence and the nucleic acid sequence which is improper under the sequence rules.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1652

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26, 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a lipoprotein associated phospholipase A2 (LPA-PLA2) having a molecular weight of from about 45-50 kDa and comprising amino acid sequence encoded by SEQ ID NO:9, does not reasonably provide enablement for any or all such LPA-PLA2 from any or all sources including polypeptides comprising fragments, variants, mutants and recombinants wherein said enzyme is encoded by a polynucleotide having at least 90% sequence identity with a human SEQ ID NO:9 or a polynucleotide having at least 90% sequence identity with nucleotides 929-1018 of a human SEQ ID NO:9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 25-26, 28 are so broad as to encompass any LPA-PLA2 from any or all sources and enzymes comprising fragments. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of LPA-PLA2s broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a

Art Unit: 1652

protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single LPA-PLA2. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the making of and use of the amino acid sequence encoded by SEQ ID NO:9 as a LPA-PLA2 but provides no guidance with regard to the making of enzymes comprising the fragments, variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function of a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

Art Unit: 1652

would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any LPA-PLA2 because the specification does not establish: (A) a rational and predictable scheme for isolating or purifying any LPA-PLA2 with an expectation of obtaining the desired biological function (B) regions of the protein structure encoded by SEQ ID NO:9 which may be modified without effecting its activity; (C) the general tolerance of LPA-PLA2s to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue on the amino acid sequence encoded by SEQ ID NO:9 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any LPA-PLA2 as stated above. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of LPA-PLA2 having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Art Unit: 1652

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

August 16, 2004